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| EXAMINER | |
|---|---|
| NEGIN, RUSSELL SCOTT | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1631 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

| Office Action Summary | Application No. | Applicant(s) |
|---|---|---|
| | 10/825,893 | YAKHINI ET AL. |
| | **Examiner** | **Art Unit** |
| | RUSSELL S. NEGIN | 1631 |

***-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on 14 November 2008.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-12 and 14-28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 and 14-28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Comments*

In view of the appeal brief filed on 14 November 2008, PROSECUTION IS HEREBY REOPENED. Additional grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Claims 1-12 and 14-28 are pending and examined in this Office action.

### *Claim Rejections - 35 USC § 101*

<u>The following rejection is newly applied under different grounds than the previous Office action</u>:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-12 and 14-28 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-11 are drawn to a method for selecting a set of normalizing data points..

As stated in MPEP 2106, section IV, if the claims are found to cover a judicial exception then the claims will be evaluated for providing a practical application of the judicial exception (*i.e.*, Law of Nature, Natural Phenomenon, or an Abstract Idea). This is in line with the recent decision in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008). In the instant case, the claims are drawn to an abstract idea and therefore must be evaluated further for providing a practical application of the judicial exception. Two of the possible ways for a practical application to result are: (1) if the claimed invention physically transforms an article or physical object to a different state or thing (a physical transformation), or (2) if the claimed invention otherwise produces a concrete, tangible, and useful result. In the instant case, a physical transformation of matter is not provided, as the instant claims merely provide steps of *in silico* information manipulation. Therefore, none of said steps result in a physical transformation of matter such that the whole of the claim is statutory.

As such, the claims must be further evaluated for providing the practical application. One way to do this is for the claim to produces a concrete, tangible and useful result. The focus is not on the steps taken to achieve a particular result, but rather the final result achieved by the claimed invention. In the instant set of claims, while the data points are stored in a memory, it is not known what real-world practical

application the data possesses from the claimed limitations. Consequently, the practical application of the instant set of claims is not apparent.

However, in addition to the facts set forth above that state that a claim must provide a practical application, the claim **must also meet** the machine-or-transformation test in order to be eligible under 35 USC 101 as statutory subject matter (*In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008). In other words, the prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept **may have a practical application,** a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (*Gottschalk v. Benson*, 409 U.S. 63, 175 USPQ 673, 1972), as clarified in *In re Bilski*, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008) the test for a method claim is whether the claimed method is (1) tied to a particular machine or apparatus <u>or</u> (2) transforms a particular article to a different state or thing.

In the instant case, the method claims are not so tied to another statutory class of invention because the **method** steps that are critical to the invention are "not tied to any **particular apparatus** or **machine**" and therefore do not meet the machine-or-transformation test as set forth in *In re Bilski* 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008).

Likewise, the corresponding system claims (claims 14-27) lack a practical application for the same reasons discussed above with respect to method claims.

Additionally claims 12 and 28 are drawn to computer instructions stored on a computer readable medium used to implement the methods described above. Since computer readable media are not defined in the specification, they are interpreted to encompass carrier waves, which are per se, not statutory.

Response to Arguments:

Applicant's arguments filed 14 November 2008 have been fully considered and they are persuasive.

In light of the recent CAFC decision of *In re Bilski* 88 USPQ.2d 1385, applicant's arguments are persuasive in that a useful, concrete, and tangible result is not required for a claim to possess a practical application (it is but one example of such a practical application). However, taking this ruling into account, it is still not known what "real-world" practical application the instant set of claims possesses. Although the specification discloses a potential use for the data normalization method in microarrays, there is no language or limitations in the instant claims associating the claimed invention with the practical application of microarray data normalization (or any biological data analysis whatsoever). In the absence of such a limitation in the claimed invention, it is not known as to what is the practical application of the invention recited in the claims.

With regard to applicant's arguments that computer readable media do not include carrier waves, applicant states on page 9 of the Brief that carrier waves are readable by computers; therefore since carrier waves are located on computers, they comprise statutory subject matter. MPEP 2106 states with regards to signals:

> The burden is on the USPTO to set forth a *prima facie* case of unpatentability. Therefore if USPTO personnel determine that it is more likely than not that the claimed subject matter falls outside all of the statutory categories, they must provide an explanation. For example, a claim reciting only a musical composition, literary work, compilation of data, >signal,< or legal document (e.g., an insurance policy) *per se* does not appear to be a process, machine, manufacture, or composition of matter. >See, *e.g.*, *In re Nuitjen*, Docket no. 2006-1371 (Fed. Cir. Sept. 20, 2007)(slip. op. at 18)("A transitory, propagating signal like Nuitjen's is not a 'process, machine, manufacture, or composition of matter.' . Thus, such a signal cannot be patentable subject matter.").< If USPTO personnel can establish a *prima facie* case that a claim does not fall into a statutory category, the patentability analysis does not end there. USPTO personnel must further continue with the statutory subject matter analysis as set forth below. Also, USPTO personnel must still examine the claims for compliance with 35 U.S.C. 102, 103, and 112.

Consequently, signals, which are readable by computers, are non-statutory.

### ***Claim Rejections - 35 USC § 103***

The following rejection is newly applied:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 7, 12, 14, 17, 20, 23, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larson et al. [Calculus with Analytic Geometry, 1990, D. C. Heath and Company; Lexington, Massachusetts; Section 14.1, pages 27-33, 785-795, and page 840] in view of Yang et al. [Nucleic Acids Research, 2002, volume 30, 10 pages starting at e15].

Claim 1 is drawn to a method for selecting a set of normalizing data points from n data sets, when n is at least 3, containing data points having values and identities, the method comprising:

--receiving n data sets;

--considering the data points to be distributed in an n-dimensional data point space;

--determining one or more order-preserving sequences of data points within the n-dimensional data point space;

--selecting, as normalizing data points, data points from the one or more order-preserving sequences; and

--storing the selected normalizing points in a computer memory as a basis for subsequence normalization of the n data sets.

Claim 7 is further limiting wherein considering the data points to be distributed in an n-dimensional data point space further includes, for each data point, considering the data point to have a value in each of n-dimensions, the value of a data point in an i-th dimension equal to the value of the data point in an i-th data set.

Claim 12 is further limiting wherein the method is in the form of computer instructions on computer readable media.

Claim 14 is drawn to the same subject matter as instant claim 1 except that it is a system on a computer.

The section of Larson et al., entitled, “Solid analytic geometry and vectors in space,” describes all of the steps if the instant method except for the use of computer memory.

In this instance, there are three dimensions, and points are distributed in three-dimensional space (see the Figures 14.1 through 14.7 on pages 785-787 of Larson et al).

Terms of interest are defined in the instant specification, on page 17, lines 11-16, and they are reiterated here for convenience:

> An order-preserving sequence us a sequence of data points in which the value of the data points within the sequence uniformly increase within the sequence. When a sequence is defined as an ordered subset of points with a data set, then a longest-order-preserving sequence (‘LOPS’) is the maximally sized, one or more ordered subsets of points selected from the data set that are ordered by signal strength or by some other associated value, parameter, or characteristic. A heaviest-order- preserving sequence (‘HOPS’) is the order preserving sequence with greatest sums of weights associated with data points in order-preserving sequence.

Consequently, when applied to three-dimensions, the method of finding order-preserving sequences of data points in the instant application (i.e. Figure 11B) involves

iteration(s) of determining traces of points in the same octant as the point before it with each subsequent point determining its own coordinate system.

Now, when taking into account limitations of instant claim 1 in combination with the rectangular solid (i.e. Figures 14.1 and 14.6); a rectangular solid in the first octant has 8 data points with the following identifiers → (0, 0, 0), (1, 0, 0), (0, 1, 0), (0, 0, 1), (1, 1, 0), (1, 0, 1), (0, 1, 1), and (1, 1, 1). Consequently, these coordinates are in three dimensional space and they encompass three data sets: X coordinates [0, 1, 0, 0, 1, 1, 0, 1], Y coordinates [0, 0, 1, 0, 1, 0, 1, 1], and Z coordinates [0, 0, 0, 1, 0, 1, 1, 1]. Consequently, the Figures of Larson illustrate three data sets in three dimensional space.

Now, the next step of determining one or more order preserving sequence in 3-dimensional space is illustrated in Figure 14.6 on page 787 of Larson et al., wherein it is shown that a vector from [0, 0, 0] to [1, 1, 1] preserves the increasing order of each data set (x coordinates, y coordinates and z coordinates). Consequently, Figure 14.6 also illustrates selection of the sequence of points [0, 0, 0] and [1, 1, 1].

Page 840 in Larson et al. illustrates storage of 3 dimensional graphic data on a computer system in order to generate graphics.

However, while Larson et al. teaches one or more sequences that maintain their LOP ordering in three dimensional space, Larson et al. does not explicitly select these data points (which may be used for normalization) and actually determine that there is a specific ordering to the given data.

The article of Yang et al. studies normalization of cDNA microarray data.

Specifically, Figure 3 of Yang et al., for example, illustrates microarray data selected for normalization wherein the order is selected and indicated by lines overlaying the actual microarray data.

Claims 4 and 17 are further limiting wherein the one or more order-preserving sequences of data points is a longest order preserving sequence of data points having a shortest Euclidean distance accumulated along a both from an initial data point of the order-preserving sequence to a final data point of the order preserving sequence.

Figure 14.6 on page 787 of Larson et al. illustrates the shortest Euclidean path between the order preserving sequences from [0 ,0 ,0] to [1, 1, 1] with a unit vector going directly from the starting to the ending point.

Claim 20 is drawn to the same subject matter as instant claim 1, with the exception the data points are considered in n/2 separate 2-dimensional data point spaces where n is as even number greater than or equal to 4.

Claim 23 is further limiting wherein the one or more order-preserving sequences of data points is a longest order preserving sequence of data points having a shortest Euclidean distance accumulated along a both from an initial data point of the order-preserving sequence to a final data point of the order preserving sequence.

Claim 28 is drawn to computer instructions stored in a computer readable medium that implements the method of claim 20.

The discussion of Larson et al. above teaches all of the limitations of instant claim 20 and 23 except the 2 (or more) separate two dimensional spaces. Page 30 of Larson et al. teaches two separate order preserving sequences in two separate 2 dimensional spaces with the shortest Euclidean distances drawn between the relevant points (i.e. Figure 1.41 and 1.42 of Larson et al.).

It would have been obvious to some one of ordinary skill in the art at the time of the instant invention to modify the vector geometric analysis of Larson et al. by use of the microarray data selection and order determination of Yang et al. wherein the motivation would have been that the analysis of Yang et al. applies the geometric coordinate analysis of Larson et al. to an actual selection and determination of an order of data on a DNA microarray (see, for example, Figure 3 of Yang et al.) There would have been a reasonable expectation of success in combining Larson et al. and Yang et al. because the general geometric analysis of Larson et al. is applicable to the normalization and ordering study of Yang et al.

It would have been obvious to some one of ordinary skill in the art at the time of the instant invention to modify the vector geometric analysis of Larson et al. by use of the computer graphics system disclosed in Larson et al. because it is obvious to improve a known technique with a known method. In this instance, it would have been obvious to automate the geometric algorithm by use of the computer system to result in a faster, more expeditious system for generating multi-dimensional graphics. There would have been a reasonable expectation of success to automate because the

graphing and automation techniques of Larson et al. are generically applicable to illustrate the geometric principles within Larson et al.

Response to Arguments:

Applicant's arguments filed 14 November 2008 have been fully considered but they are not persuasive.

Applicant first argues on page 13 of the Brief that while the calculus textbook is relevant to “continuous mathematics,” the mathematics recited in the instant set of claims is “discrete mathematics.” This argument is not persuasive because while calculus is related to continuous mathematics, the specific cited portion of the textbook is a review of the discrete mathematics germane to three dimensional analytical geometry and vector space. In other words, just because the subject of the textbook of Larson et al. is calculus does not mean that every principle within the book is necessarily continuous calculus mathematics; portions of the textbook (i.e. the cited portion) is a review of geometry.

Applicant next argues on pages 13-14 of the Brief that Larson et al. has nothing to do with "receiving n data sets." In this argument applicant cites a portion of the specification describing the use of data. This passage states:

> Data points, or features, in a number of microarray data sets have both identities and values. The values of a data point ***are generally*** a measure of scanned intensities of light or radiation emitted from labeled target molecules bound to the feature, and the identity ***may be*** two-coordinate indexes, a sequence number, or an alphanumeric label that unqiuely identifies the feature within the data set. A data point ***may*** also, in certain cases, be associated with a weight, where the weight expressed a measure of confidence, constancy, or some other parameter or characteristic.

Consequently, while these exemplary embodiments of the specification are useful in describing specific examples of data, this passage is not a limiting definition of data points. Although on page 14 of the Brief, applicant disputes the notion that coordinates in the figures of Larson et al. by themselves are not data, applicant has provided no evidence or support from the specification, that such numerical information within Larson et al. may NOT be interpreted as data. Conversely, the passage cited by applicant above supports that the points in figures 14.1 to 14.6 of Larson et al. are data with alphanumeric labels (i.e. each point is a three dimensional coordinate and some of the points have alphanumeric labels such as P and Q).

Applicant continues to argue on pages 14-15 of the Brief that Larson et al. describes only ABSTRACT mathematical concepts and not practical data points. However, in the absence of a specific definition of “data” or “data points,” while claims are read in light of the specification, the exemplary embodiments (such as microarray applications) can not be “read into” the claims.

Applicant argues on page 16 of the Brief that Figure 14.1 of Larson et al. is not a rectangular solid and that Figure 14.6 of Larson et al. shows a vector in three-dimensional vector space. Applicant argues that the coordinates in Figure 14.1 and 14.6 and the X, Y, and Z data sets cited in the previous non-Final Office action have nothing to do with data sets, but instead points in three dimensional space. These arguments are not persuasive, because the combination of Figure 14.1 and Figure 14.6 of Larson et al. teach a lowest order preserving sequence between two data points. The data sets cited in the previous Office action were merely intended to illustrate that

the order is preserved in each of the three dimensions between the first point in three dimensional space and the second point. Furthermore, the vector in Figure 14.6 reinforces the direction between he two points in the first octant of the vector space (i.e. the vector illustrates an increase in the data values in each of the three dimensions).

Applicant next argues on page 17 of the Brief that Figure 14.6 of Larson et al. has been misconstrued and that the vector for [0,0,0] to [1,1,1] is not a unit vector. While applicant is correct in that the vector from [0,0,0] to [1,1,1] is not a unit vector, there is no recitation of a unit vector in the instantly rejected claims. In other words, each of the four vectors in Figure 14.6 of Larson et al. is a unit vector as required by the caption such that the endpoint of vector v must be in the first octant of three dimensional space. However, vector v is STILL a lowest order preserving sequence between two data points because the vector v points from the origin of the coordinate system to a point in the first octant such that all of the values v1, v2, and v2 are positive and the order between each dimension is maintained and increasing. Additionally, as an aside, the instant rejected claims do not recite any normalization process; only normaliz**ing** (and NOT normaliz**ed**) data are used.

Applicant continues to argue on page 18 of the Brief that Figures 10A and 11A of the instant disclosure exemplify the concept or LOPS as requiring experimentally determined and not abstract values. This is not persuasive because, again, there is no limitation recited in the claims, nor are there limiting definitions in the specification (or Figures) limiting the data to empirical or experimental data.

Applicant continues to argue on pages 18-19 of the Brief alleged differences between continuous and discrete mathematics and vectors in three-dimensional space. These arguments have been addressed above.

## *Conclusion*

No claim is allowed.

Claims 2-3, 5-6, 8-11, 15-16, 18-19, 21-22, and 24-28 are free of the prior art for the following reasons.

Claims 2, 15, and 21 are free from the prior art, because while Larson et al. teaches the "shortest" order preserving sequence (i.e. the distance minimizing the Euclidean distance between points), the prior art does not show the “longest” order preserving sequences between data points.

Claims 3, 6, 16, 19, 22, and 25 are free of the prior art because the art does not teach weighting order preserving sequences and then summing these weights.

Claims 5, 6, 9, 18, 19, 24, 25, and 27 are free of the prior art because the art does not teach thresholds to associate with the order preserving sequences.

Claims 8-11 and 26 are free of the prior art because the art does not teach determining metrics of ordering preserving sequences by traversing in independent directions in multidimensional space.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices

published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin
6 February 2008

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631